General

Guideline Title

WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders.

Bibliographic Source(s)

World Health Organization (WHO). WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. Geneva (Switzerland): World Health Organization (WHO); 2012. 34 p. [92 references]

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Ratings schemes for the quality of evidence (high, moderate, low, very low) and the strength of the recommendations (strong, conditional [weak]) are defined at the end of the "Major Recommendations" field.

Establish and Strengthen the Mechanisms for Delivering Integrated Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) Services

Set Up and Strengthen a Coordinating Body for Collaborative TB/HIV Activities Functional at All Levels

Recommendations

1. HIV programmes and TB-control programmes or their equivalents should create and strengthen a joint national TB/HIV coordinating body, functional at regional, district, local and facility levels (sensitive to country-specific factors), with equal or reasonable representation of the two programmes including of people at risk of or affected by both diseases, and other line ministries (e.g., working on harm reduction and prison or mining health services).
2. The TB/HIV coordination bodies should be responsible for the governance, planning, coordination and implementation of collaborative TB/HIV activities as well as mobilization of financial resources.

Determine HIV Prevalence among TB Patients and TB Prevalence among People Living with HIV

Recommendations

1. Surveillance of HIV should be conducted among TB patients and surveillance of active TB disease among people living with HIV in all countries, irrespective of national adult HIV and TB prevalence rates, in order to inform programme planning and implementation.
2. Countries with unknown HIV prevalence rates among TB patients should conduct a seroprevalence (periodic or sentinel) survey to assess the situation.
3. In countries with a generalized epidemic state (HIV prevalence is consistently >1% in pregnant women), HIV testing and counselling of all patients with presumptive or diagnosed TB should form the basis of surveillance. Where this is not yet in place, periodic surveys or sentinel surveys are suitable alternatives.
4. In countries with a concentrated epidemic state (HIV prevalence is consistently >5% in at least one defined subpopulation and is <1% in pregnant women in urban areas) where groups at high risk of HIV infection are localized in certain administrative areas, HIV testing and counselling of all patients with presumptive or diagnosed TB in those administrative areas should form the basis of surveillance. Where this is not yet in place, periodic (special) or sentinel surveys every 2–3 years are suitable alternatives.
5. In countries with a low-level epidemic state (HIV prevalence has not consistently exceeded 5% in any defined subpopulation), periodic (special) or sentinel surveys are recommended every 2–3 years.
6. HIV testing should be an integral part of TB prevalence surveys and antituberculosis drug resistance surveillance.

Carry Out Joint TB/HIV Planning to Integrate the Delivery of TB and HIV Services

Recommendations

1. Joint planning should clearly define the roles and responsibilities of HIV and TB control programmes in implementing, scaling-up and monitoring and evaluating collaborative TB/HIV activities at all levels of the health system.
2. HIV programmes and TB-control programmes should describe models to deliver client and family-centred integrated TB and HIV services at facility and community levels compatible with national and local contexts.
3. HIV programmes and TB-control programmes should ensure resource mobilization and adequate deployment of qualified human resources to implement and scale-up collaborative TB/HIV activities in accordance with country-specific situations.
4. HIV programmes and TB-control programmes should formulate a joint training plan to provide preservice and in-service training, and continuing competency-based education on collaborative TB/HIV activities for all categories of health-care workers. Job descriptions of health workers should be developed and/or adapted to include collaborative TB/HIV activities.
5. HIV programmes and TB-control programmes should ensure that there is sufficient capacity to deliver health care (e.g., adequate laboratories, supplies of medicines, referral capacity, private sector involvement, focus on key populations such as women, children, people who use drugs and prisoners) and effectively implement and scale up collaborative TB/HIV activities.
6. HIV programmes and TB-control programmes should develop specific strategies to enhance the involvement of nongovernmental and other civil society organizations and individuals affected by or at risk of both diseases in developing and implementing policy and programmes, and the monitoring and evaluation of collaborative TB/HIV activities at all levels.
7. Well designed TB/HIV advocacy activities that are jointly planned to ensure coherence between their messages and targeted at key stakeholders and decision-makers, should be carried out at global, national, regional and local levels.
8. The joint communication strategies should ensure the mainstreaming of HIV components in TB communication and of TB components in HIV communication.
9. All stakeholders of collaborative TB/HIV activities, including HIV programmes and TB-control programmes, should support and encourage operational research on country-specific issues to develop the evidence base for efficient and effective implementation of collaborative TB/HIV activities.

Monitor and Evaluate Collaborative TB/HIV Activities

Recommendations

1. HIV programme and TB-control programmes should establish harmonized indicators and standard reporting and recording templates to collect data for monitoring and evaluation of collaborative TB/HIV activities.
2. Organizations implementing collaborative TB/HIV activities should embrace harmonized indicators and establish a reporting mechanism to ensure that their data are captured by the national monitoring and evaluation system of the country.
3. The WHO guide to monitoring and evaluation of collaborative TB/HIV activities and the three interlinked patient monitoring systems for HIV care/antiretroviral therapy (ART), maternal and child health (MCH)/prevention of mother-to-child transmission (PMTCT) and TB/HIV should be used as a basis to standardize country-specific monitoring and evaluation activities.

Reduce the Burden of TB among People Living with HIV and Initiate Early Antiretroviral Therapy (*the Three Is for HIV/TB*)

Intensify TB Case-Finding and Ensure High-Quality Antituberculosis Treatment

Recommendations

1. Adults and adolescents living with HIV should be screened for TB with a clinical algorithm; those who report any one of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB and other diseases (strong recommendation, moderate quality of evidence).
2. Children living with HIV who have any of the following symptoms – poor weight gain, fever or current cough or contact history with a TB case – may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, children should be offered isoniazid preventive therapy (IPT) regardless of their age (strong recommendation, low quality of evidence).
3. TB patients with known positive HIV status and TB patients living in HIV-prevalent settings should receive at least 6 months of rifampicin treatment regimen (strong recommendation, high quality of evidence). The optimal dosing frequency is daily during the intensive and continuation phases (strong recommendation, high quality of evidence).

Initiate TB Prevention with Isoniazid Preventive Therapy and Early Antiretroviral Therapy

Recommendations

1. Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT (strong recommendation, moderate quality of evidence).
2. Adults and adolescents who are living with HIV, have unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least 6 months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals irrespective of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women (strong recommendation, high quality of evidence).
3. Adults and adolescents living with HIV who have an unknown or positive TST status and who are unlikely to have active TB should receive at least 36 months of IPT. IPT should be given to such individuals irrespective of the degree of immunosuppression, and also those on ART, those who have previously been treated for TB and pregnant women (conditional recommendation, moderate quality of evidence).
4. TST is not a requirement for initiating IPT in people living with HIV (strong recommendation, moderate quality of evidence). People living with HIV who have a positive TST benefit more from IPT; TST can be used where feasible to identify such individuals (strong recommendation, high quality of evidence).
5. Providing IPT to people living with HIV does not increase the risk of developing isoniazid-resistant TB. Therefore, concerns regarding the development of INH resistance should not be a barrier to providing IPT (strong recommendation, moderate quality of evidence).
6. Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB (strong recommendation, low quality of evidence).
7. Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care services (strong recommendation, moderate quality of evidence).
8. In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months IPT if the evaluation shows no TB disease (strong recommendation, low quality of evidence).
9. All children living with HIV after successful completion of treatment for TB disease should receive isoniazid for an additional 6 months (conditional recommendation, low quality of evidence).
10. All people living with HIV with CD4 counts of $\leq$350 cells/mm^3 irrespective of the WHO clinical stage should start ART (strong recommendation, moderate quality of evidence).

Ensure Control of TB Infection in Health-Care Facilities and Congregate Settings

Recommendations

1. HIV programmes and TB-control programmes should provide managerial direction at national and subnational levels for the implementation of TB infection control in health-care facilities and congregate settings.
2. Each health-care and congregate setting should have a TB infection control plan of the facility, preferably included into a general infection control plan, supported by all stakeholders, which includes administrative, environmental and personal protection measures to reduce transmission of TB in health-care and congregate settings, and surveillance of TB disease among workers.
3. Health-care workers, community health workers and care providers living with HIV should be provided with ART and IPT if eligible. Furthermore, they should be offered an opportunity for transfer to work in clinical sites that have the least risk of TB transmission.

Reduce the Burden of HIV in Patients with Presumptive and Diagnosed TB

Provide HIV Testing and Counselling to Patients with Presumptive and Diagnosed TB

Recommendations

1. Routine HIV testing should be offered to all patients with presumptive and diagnosed TB (strong recommendation, low quality of evidence).
2. Partners of known HIV-positive TB patients should be offered voluntary HIV testing and counselling with mutual disclosure (strong recommendation for all people with HIV in all general HIV epidemic settings).
3. TB-control programmes should mainstream provision of HIV testing and counselling in their operations and routine services.

Introduce HIV Prevention Interventions for Patients with Presumptive and Diagnosed TB

Recommendations

1. TB-control programmes should implement comprehensive HIV prevention strategies for their patients and their partners, targeting sexual, parenteral or vertical transmission or should establish a referral linkage with HIV programmes to do so.
2. HIV programmes and TB-control programmes should implement procedures for voluntary, acceptable and confidential HIV counselling and testing for health-care providers and for education of occupational and nosocomial exposure to HIV infection in their services.
3. All personnel working with presumptive and confirmed TB cases, people living with HIV and people who use drugs should be able to assess risk factors for HIV infection and transmission and should provide comprehensive information and services to their clients to minimize their risks.
4. HIV programmes and TB-control programmes should collaborate with harm reduction services to ensure universal access to comprehensive TB and HIV prevention, diagnosis, treatment and care as well as drug treatment services, including opioid substitution therapy, for people who use drugs in a holistic person-centred approach to maximize access and adherence within one setting as much as possible.
5. TB-control programmes should ensure that vertical transmission of HIV is prevented by referring all HIV-positive pregnant women attending TB services to providers of services for prevention of vertical transmission of HIV for antiretroviral therapy or prophylaxis as needed.

Provide Co-trimoxazole Preventive Therapy (CPT) for TB Patients Living with HIV

Recommendation

1. Routine CPT should be administered in all HIV-infected patients with active TB disease regardless of CD4 counts (strong recommendation, high quality of evidence).

Ensure HIV Prevention Interventions, Treatment and Care for TB Patients Living with HIV

Recommendations

1. All people living with HIV who are diagnosed with TB should receive integrated services for prevention, diagnosis, treatment and care of TB and HIV.
2. HIV programmes and TB-control programmes should ensure access to a continuum of comprehensive and integrated prevention, care and treatment for people living with HIV who are receiving or who have completed their antituberculosis treatment.

Provide Antiretroviral Therapy for TB Patients Living with HIV

Recommendations

1. ART should be started in all TB patients living with HIV irrespective of their CD4 counts (strong recommendation, low quality of evidence).

2. Antituberculosis treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, moderate quality of evidence). Those HIV-positive TB patients with profound immunosuppression (e.g., CD4 counts less than 50 cells cells/mm^3) should receive ART immediately within the first 2 weeks of initiating TB treatment.
3. Efavirenz should be used as the preferred non-nucleoside reverse transcriptase inhibitor in patients starting ART while on antituberculosis treatment (strong recommendation, high quality of evidence).

National Targets for Scaling Up Collaborative TB/HIV Activities

Recommendation

Countries implementing collaborative TB/HIV activities should set their own country-specific process and impact targets for scaling up collaborative TB/HIV activities towards achieving the Millennium Development Goals.

Definitions:

Strength of the Recommendation

Strength of Recommendation	Rationale
Strong	The panel is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.
Conditional (weak)	The panel concludes that the desirable effects of adherence to the recommendation probably outweigh the undesirable effects. However: • Data to support the recommendation are scant; or • The recommendation is only applicable to a specific group, population or setting; or • New evidence may result in changing the balance of risk to benefit; or • The benefits may not warrant the cost or resource requirements in all settings.

Levels of Assessment of the Evidence

Evidence	Rationale
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the effect.
Low	Further research is very likely to have an estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Human immunodeficiency virus (HIV)
- Tuberculosis (TB)

Guideline Category

Counseling

Diagnosis

Management

Prevention

Screening

Treatment

Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Nursing

Obstetrics and Gynecology

Pediatrics

Preventive Medicine

Psychology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Patients

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Public Health Departments

Social Workers

Utilization Management

Guideline Objective(s)

- To provide national programmes and stakeholders with guidelines on how to implement and scale-up collaborative tuberculosis (TB)/human immunodeficiency virus (HIV) activities
- To establish and strengthen the mechanisms of collaboration and joint management between HIV programmes and TB-control programmes for delivering integrated TB and HIV services preferably at the same time and location
- To reduce the burden of TB in people living with HIV, their families and communities by ensuring the delivery of the Three I's* for HIV/TB and the early initiation of antiretroviral therapy (ART) in line with World Health Organization (WHO) guidelines
- To reduce the burden of HIV in patients with presumptive and diagnosed TB, their families and communities by providing HIV prevention, diagnosis and treatment

*Intensify TB case-finding and ensure high-quality antituberculosis treatment; initiate TB prevention with isoniazid preventive therapy and early antiretroviral therapy; ensure control of TB Infection in health-care facilities and congregate settings

Target Population

People at risk of or affected by tuberculosis (TB) and human immunodeficiency virus (HIV) infection

Interventions and Practices Considered

1. Creating and strengthening a joint national tuberculosis/human immunodeficiency virus (TB/HIV) coordinating body
2. Surveillance and testing to determine HIV prevalence among TB patients and TB prevalence among people with HIV
3. Joint TB/HIV planning to integrate delivery of TB and HIV services
4. Monitoring and evaluating collaborative TB/HIV activities
5. TB case-finding and ensuring high-quality antituberculosis treatment
6. TB prevention with isoniazid preventive therapy
7. Initiating early antiretroviral therapy in people living with HIV
8. Ensuring control of TB infection in health-care facilities and congregate settings
9. Providing HIV testing and counselling to patients with presumptive and diagnosed TB
10. Implementing HIV prevention interventions for patients with presumptive and diagnosed TB
11. Providing co-trimoxazole preventive therapy (CPT) for TB patients living with HIV
12. Providing antiretroviral therapy for TB patients living with HIV
13. Setting national targets for scaling up collaborative TB/HIV activities

Major Outcomes Considered

- Rate of tuberculosis (TB) diagnosis
- Rate of human immunodeficiency virus (HIV) diagnosis
- Reduction in morbidity and mortality from TB and/or HIV
- Rate of hospitalization
- Rate of adverse events leading to hospitalization or treatment discontinuation

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Systematic literature reviews of studies related to four questions (see the "Description of the Methods Used to Analyze the Evidence" field) were conducted using PubMed, MEDLINE, EMBASE and various other databases using combinations of different keywords to search for studies related to each question. A search was also conducted for abstracts presented at conferences on tuberculosis (TB) and lung diseases organized by the International Union Against Tuberculosis and Lung Disease (The Union) and the International AIDS Society. Investigators of large-scale human immunodeficiency virus (HIV) clinical trials were also asked for information, especially about the role of earlier initiation of antiretroviral therapy (ART) to prevent TB. All retrieved titles and abstracts were reviewed for their relevance to the topic in question. The reference lists of the retrieved studies were also reviewed to identify further studies that met the eligibility criteria. In addition, recognized experts in the field were contacted to identify any unpublished studies that did not appear in the initial electronic search for each question.

Search Criteria and Selection for Clinical Questions

Population, Intervention, Comparison, Outcomes (PICO) Question 1

Can earlier initiation of antiretroviral therapy (ART) at higher CD4 counts (>350 cells/mm^3) be used to prevent active TB in people living with HIV? Should antiretroviral therapy be used to prevent active tuberculosis?

Population: adults and adolescents living with HIV
Intervention: ART at CD4 counts >350 cells/mm^3
Comparison: no ART or ART deferred until CD4 counts ≤350 cells/mm^3
Outcomes: TB incidence rate

Literature Search Strategy and Information Retrieval

Studies were identified using PubMed and the Cochrane Library databases. No systematic reviews were identified using the Cochrane database.

Selection Criteria

Studies were selected if:

- Randomized and quasi-randomized controlled studies, including historically controlled trials or observational and cohort studies
- Participants were people living with HIV
- Incidence rates for both exposure groups of PICO question were given

See Annex 1 of the original guideline document for more details (see the "Availability of Companion Documents" field).

PICO Question 2

What are the benefits of HIV testing and counselling in patients with presumptive and diagnosed TB and among the partners and family members of patients who are found to be HIV-positive?

Population: people with presumptive and diagnosed TB, and the partners and family members of patients who are found to be HIV positive
Intervention: HIV testing and counselling
Comparison: no HIV testing and counselling
Outcomes: yield of positive HIV cases

Literature Search Strategy and Information Retrieval

Studies were identified using PubMed, EMBASE, Web of Science, Google Scholar and the Cochrane Library databases. Proceedings and abstracts from international conferences (Conference on Retroviruses and Opportunistic Infections [CROI], International AIDS Society [IAS], Interscience Conference on Antimicrobial Agents and Chemotherapy [ICAAC], World AIDS Conference) were searched.

Selection Criteria

Studies were included if:

- Randomized and quasi-randomized controlled trials, including historically controlled trials or observational and cohort studies

- Participants being presumed or confirmed TB cases or/and partners and family members of those who turn to be HIV positive
- Comparison being addressed was: routine HIV testing vs. no HIV testing

See Annex 2 of the original guideline document for more details (see the "Availability of Companion Documents" field).

PICO Question 3

Does the administration of routine co-trimoxazole preventive therapy (CPT) compared with no CPT reduce the number of illness episodes and deaths in TB patients living with HIV?

Population: TB patients living with HIV
Intervention: CPT
Comparison: no CPT or placebo
Outcomes: mortality, morbidity/hospital admissions/adverse events

Literature Search Strategy and Information Retrieval

Studies were identified using PubMed, EMBASE, Web of Science, Google Scholar and the Cochrane Library databases. Proceedings and abstracts from international conferences (CROI, IAS, ICAAC, World AIDS Conference) were searched.

Selection Criteria

Studies were selected if:

- Randomized and quasi-randomized controlled trials, including historically controlled trials or observational and cohort studies
- Participants being people living with HIV with active TB (studies that include participants both with and without active TB disease were considered where the data for those with TB disease could be extracted)
- Comparison being addressed was: routine CPT vs. placebo or no CPT

See Annex 3 of the original guideline document for more details (see the "Availability of Companion Documents" field).

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Assessment of the Evidence

Evidence	Rationale
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the effect.
Low	Further research is very likely to have an estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The following four questions (three clinical and one programmatic) that were not covered by the 11 guideline documents used to update the policy (see Section 1.4 in the original guideline document) were identified by the Steering Group and a comprehensive systematic review of the available scientific evidence was conducted to formulate the related recommendations.

1. What are the benefits of HIV testing and counselling among patients with presumptive TB (that is, patients with signs and symptoms of TB or suspected TB) and diagnosed TB, and the partners and family members of those found to be HIV-positive?
2. Does the administration of routine co-trimoxazole preventive therapy, as compared with no co-trimoxazole preventive therapy, reduce the number of illness episodes and deaths in TB patients living with HIV?
3. Can earlier initiation of antiretroviral therapy at higher CD4 counts (more than 350 cells/mm^3) be used to prevent active TB in people living with HIV?
4. What models are available to deliver integrated TB and HIV services for people living with HIV?

The quality of evidence and the strength of each recommendation were assessed using the Grading Recommendations Assessment, Development and Evaluation (GRADE) methodology for clinical questions 1–3. In the GRADE assessment process, the quality of a body of evidence is defined as the extent to which one can be confident that the reported estimates of effect (desirable or undesirable) available from the evidence are close to the actual effects of interest. The usefulness of an estimate of the effect (of the intervention) depends on the level of confidence in that estimate. The higher the quality of evidence, the more likely a strong recommendation can be made; however, the decision regarding the strength of the evidence also depends on other factors. Although the GRADE evidence assessment process was used for the clinical questions, it was not always possible to complete GRADE profiles for all the questions because there was a lack of data and information to calculate the necessary risk ratios.

The strength of evidence and recommendation is presented for the three clinical questions that were specifically reviewed for the development of this policy. The strength of evidence and recommendation from the other documents approved by the GRC are also presented when possible. However, given the lack of the data necessary to calculate risk ratios, and as they largely represent programmatic processes, the strength of evidence for the activities included in the "Establish and Strengthen the Mechanisms for Delivering Integrated TB and HIV Services" section (see the "Major Recommendations" field) of the collaborative TB/HIV activities and for the programmatic question (4 above) is not presented.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The process of updating the policy followed that recommended by the World Health Organization (WHO) Guidelines Review Committee (GRC). A WHO Steering Group and a Policy Updating Group comprising policy-makers, programme managers, tuberculosis (TB) and human immunodeficiency virus (HIV) experts, donor agencies, civil society organizations including people living with HIV, and a methodologist in Grading of Recommendations Assessment, Development and Evaluation (GRADE) were established to oversee the process and develop recommendations. The policy guidelines build on the basic framework of the interim policy document that structured collaborative TB/HIV activities under three distinct objectives (establishing and strengthening the mechanisms for delivering integrated TB and HIV services, reducing the burden of TB among people living with HIV, and reducing the burden of HIV among people diagnosed with or presumed to have TB).

Recommendations from 11 documents that were approved by the GRC were used to update the policy (see Section 1.4 of the original guideline document).

The draft document, including the population/intervention/comparison/outcome (PICO) questions, was prepared by a WHO Steering Group, representing the WHO HIV/AIDS and Stop TB departments, and then circulated to the members of the Policy Updating Group for feedback. The group discussed the overall structure of the policy through email-based discussion, assessed the evidence along with the risks and benefits of the three clinical questions, and determined the recommendations and their strengths. A telephone conference call was organized among members of the Policy Updating Group to further discuss issues that were not clarified during the email-based discussions. The policy was revised based on

feedback obtained from emails and telephone conference discussion and reviewed again by the Policy Updating Group before consensus was reached.

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendation

Strength of Recommendation	Rationale
Strong	The panel is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.
Conditional (weak)	The panel concludes that the desirable effects of adherence to the recommendation probably outweigh the undesirable effects. However: • Data to support the recommendation are scant; or • The recommendation is only applicable to a specific group, population or setting; or • New evidence may result in changing the balance of risk to benefit; or • The benefits may not warrant the cost or resource requirements in all settings.

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The policy was circulated to 34 internal and external peer reviewers. Comments from internal and external peer reviewers were discussed among the World Health Organization (WHO) Steering Group, and the document was finalized by the coordinators of the process.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Effective and efficient coordination of testing, treating, counseling, and following people at risk for or affected by tuberculosis (TB) and human immunodeficiency virus (HIV)

Potential Harms

- Caution is needed in people living with human immunodeficiency virus (HIV) with tuberculosis (TB) meningitis as immediate antiretroviral therapy (ART) was significantly associated with more severe adverse events when compared with initiation of ART 2 months after the start of antituberculosis treatment.
- Patients should be closely followed-up to assess the occurrence of side-effects related to co-treatment and of TB-associated immune reconstitution inflammatory syndrome (IRIS), which is common in patients with TB started on ART but usually self-limited.
- Rifampicin reduces drug levels of both nonnucleoside reverse transcriptase inhibitors and protease inhibitors through induction of the cytochrome P450 liver enzyme system. A randomized controlled trial in Thailand comparing efavirenz and nevirapine-based ART in HIV-infected TB patients receiving rifampicin showed that both standard doses of efavirenz and nevirapine were effective in achieving viral load suppression. However, reports of efficacy, safety and tolerability of efavirenz and nevirapine administered with rifampicin varied across observational studies. When rifampicin is given with protease inhibitors, highly variable and mainly subtherapeutic plasma concentrations of the protease inhibitor are observed, even in the presence of boosted doses of ritonavir.
- A concern with TB and HIV services provided at a single facility at the same time and location is the risk of nosocomial spread of TB. It should be noted however that the risk of TB transmission is not unique to this model, as it exists in general waiting areas of all health facilities in high burden settings (wherever coughing patients with undiagnosed pulmonary TB are regularly presenting).

Qualifying Statements

Qualifying Statements

- The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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Implementation of the Guideline

Description of Implementation Strategy

The interim policy on collaborative tuberculosis (TB)/human immunodeficiency virus (HIV) activities has been widely implemented since its publication in 2004. National programmes and other stakeholders should use the experiences garnered over the years to adapt their policies with the update to best suit their local circumstances. Factors should include the epidemiology of TB and HIV and the health-care delivery system specific to individual countries. The adaptation process should include national-level policy and programmatic decisions to determine the best country-specific programme management mechanism for providing integrated TB and HIV services. The ultimate goal of the adaptation should be scaled up nationwide coverage of collaborative TB/HIV activities to reduce HIV-associated TB mortality and morbidity depending on the epidemiology of TB and HIV.

Implementation Tools

Foreign Language Translations

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

World Health Organization (WHO). WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. Geneva (Switzerland): World Health Organization (WHO); 2012. 34 p. [92 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012

Guideline Developer(s)

World Health Organization - International Agency

Source(s) of Funding

The development of these guidelines was financially supported by the Joint United Nations Programme on HIV/AIDS Unified Budget and Workplan (UNAIDS UBW) and the US President's Emergency Plan for AIDS Relief (PEPFAR) through the United States Centers for Disease Control and Prevention (CDC) and the United States Agency for International Development (USAID). Partial support for the systematic reviews on TB and HIV service integration was provided by the Global Fund to Fight AIDS, TB and Malaria.

Guideline Committee

World Health Organization Steering Group and Policy Updating Group

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

All members of the Policy Updating Group were asked to complete a World Health Organization (WHO) *Declaration of interests for WHO consultants* form. Five members of the group declared a conflict of interest. Constance Benson declared consulting, scientific and technical advisory work on antiretroviral therapy new drug development with Merck, GlaxoSmithKline and ViiV for less than US$5000 each. Pedro Cahn declared ongoing research support and consulting work with Abbott for an amount of US$3000. He declared receiving US$2000 from Bristol-Myers Squibb and US$2000 from Tibotec for serving on a speakers' bureau. He also declared scientific advisory work for Merck, Pfizer, GlaxoSmithKline and Avexa for an amount of US$2000 each. Mark Harrington declared giving testimony to the Institute of Medicine of the United States National Academies in panels on multidrug-resistant tuberculosis (TB) in 2008 and 2009. Charles Holmes declared employment by Gilead up to January 2008 in the clinical research unit focusing on phase I studies of experimental antiretroviral drugs. He declared no financial or other interest in Gilead. Salim S. Abdool Karim declared receiving US$2500 from Merck to attend the advisory panel meeting on microbicides in March 2011. The declared conflicts of interest were discussed within the WHO Steering Group and with the Policy Updating Group before deliberations on the policy document, and it was concluded that these conflicts would not prohibit any of the members from participating in the process.

Declarations of interest were collected from all non-WHO reviewers. Four peer reviewers declared potential conflicts of interest. Helen Ayles declared an ongoing research grant for her research unit with Delft Diagnostic Systems of €100,000 to develop a computer-aided diagnostic for reading digital chest X-rays as well as having received a digital chest X-ray unit for an amount of US$250,000. François Boillot declared being the owner, director of and employed by a consulting company providing services in international health including in TB/HIV issues. Susan Swindells declared consulting services (advisory board) with Pfizer in 2008 (US$1800) and 2009 (US$1750), with Merck in 2009 (US$3500), with Tibotec in 2009 (US$1500) and with Abbott Molecular in 2010 (US$1000). She also declared previous research support to her institution from Bristol-Myers Squibb that ended in 2010 (US$14,929), from Pfizer that ended in 2011 (US$ 28125) and ongoing research support from GlaxoSmithKline for an amount of US$104,034 and US$60,676. Jay K. Varma declared non-monetary support (supplies and equipment) in 2010 valued at approximately US$10,000 from Cellestis to the government research unit of China and collaborators in Inner Mongolia to examine the prevalence of TB in health-care workers in collaboration with the United States Centers for Disease Control and Prevention. The WHO Steering Group discussed these declarations and concluded that they would not exclude the reviewers from the process. All declarations of conflict of interests are retained on electronic file by the WHO Stop TB Department.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) in English, French, Russian, and Spanish from the World Health Organization Web site .

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

Availability of Companion Documents

The following are available:

WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. Annexes. Geneva (Switzerland): World Health Organization (WHO); 2012. 40 p. Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization (WHO) Web site .

WHO handbook for guideline development. Geneva (Switzerland): World Health Organization (WHO); 2008 Mar. 41 p. Electronic copies: Available in PDF from the WHO Web site .

An executive summary is available in the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 9, 2012. This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on Opioid pain medicines.

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